REMARKS

Claims 1-18 are pending in the instant application. Claims 1-4 and 10-15 have been rejected by the Examiner. Claims 5, 7-9 and 16-18 have been objected to by the Examiner.

By the above amendments Claims 1, 2, 3, 4, 8 and 14 have been amended to more particularly point out and distinctly claim the subject matter which Applicants regard as the invention. More particularly, Claims 1-4 and 8 have been amended to limit the claims to the elected invention and Claim 14 amended to correct an unintentional error in dependency. Claim 6 has been canceled without prejudice.

Applicants submit that the amendments canceling claim 6 and amending the scope of claims 1-4 and 8 are being made solely to advance the prosecution of the instant application and are not in any way to be construed as an admission that the canceled material is unpatentable. Thus, Applicants reserve the right to pursue coverage of the canceled material by filing a continuation or a divisional application at an appropriate time in the future.

Applicants submit that the amendments are fully supported by the specification as filed, and no new matter is being added. After entry of the amendments, Claims 1-5 and 7-18 will remain pending and under consideration.

Reconsideration of the captioned application based on the previous amendments and following remarks is respectfully requested.

The Examiner asserts that the instant application contains claims directed to patentably distinct species of the claimed invention and has required Applicants to elect a single disclosed species under 35 U.S.C. §121.

In the Office Action, restriction was required in the above-referenced application to one of the following groups:

Groups I. Claims 5, 9 and claims 1-4, 7-8, 10-18 in part, drawn to a compound wherein X is CH, or $C(C_{1-6}alkyl)$, R^3 is aryl, aralkyl, classified in class 546, subclass 226, the composition and method of use thereof.

Group II. Claims 1-4, 7-8, 10-18 in part, drawn to a compound not included in group I, wherein X is CH, or $C(C_{1-6}alkyl)$, R^3 is other than aryl, aralkyl, classified in class 546, subclass 194, the composition and method of use thereof.

Group III. Claim 6 and claims 1-4, 7-8, 10-18 in part, drawn to a compound wherein X=N, R^3 is aryl, aralkyl, classified in class 544, subclass 358, the composition and method of use thereof.

Group IV. Claims 1-4, 7-8, 10-18 in part, drawn to a compound not included in group II, wherein X=N, R^3 is other than aryl or aralkyl, classified in class 544, subclass 360, the composition and method of use thereof.

Applicants hereby affirm the election of the invention of Group I, claims 5, 9 and claims 1-4, 7-8 and 10-18 in part made during the telephone conversation with the Examiner on January 21, 2003. In order to advance prosecution, Applicants have amended the claims to limit the invention to the elected invention of Group I.

Since Applicants have elected Group I, the Examiner has suggested that Applicants elect a species. Applicants hereby affirm the election of the species of compound #10 (page 87, Table 2). This election of species is without traverse to the extent that it is understood that (a) the requirement will be withdrawn upon the finding of an allowable genus; and (b) any species withdrawn from consideration will be transferred to the elected subject matter unless it is found patentably distinct from the elected or allowed claims.

The Examiner has rejected Claim 14 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. More particularly, the Examiner states "The method claim 14 is improperly dependent on the composition claim 10."

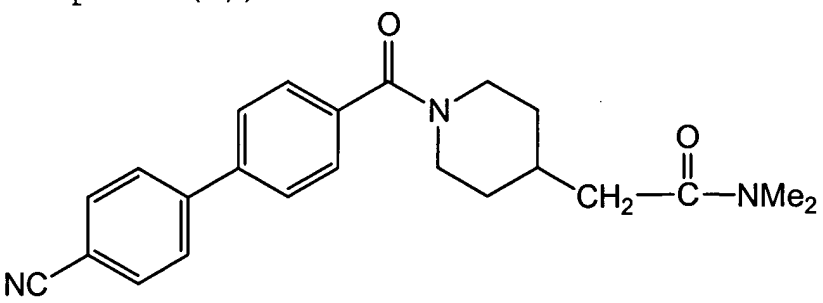
Applicants kindly refer the Examiner to the above Amendment which corrects the unintentional dependency error. Applicants respectfully request that the rejection of Claim 14 under 35 U.S.C. §112, second paragraph be withdrawn.

The Examiner has objected to Claim 11 under 37 C.F.R. 1.75 as being a substantial duplicate of claim 10.

Applicants respectfully traverse this rejection. Applicants submit that claims 10 and 11 are directed to a pharmaceutical composition and a product by process composition, respectfully. As such the claims are not substantial duplicate claims, as they are not so close in content that they cover the same thing/invention. Applicants therefore respectfully request that the objection to claim 11 as a substantial duplicate of claim 10 be withdrawn.

The Examiner has rejected Claims 1-4 and 10-12 under 35 U.S.C. §103(a) as unpatentable over Himmelsbach (USPN 5,736,559). More particularly, the Examiner states that:

> "Himmelsbach generically discloses an aggregation-inhibiting compound and the composition thereof (columns 1-2). A specific example, having the following structure is described (column 34, Example 1 (6))

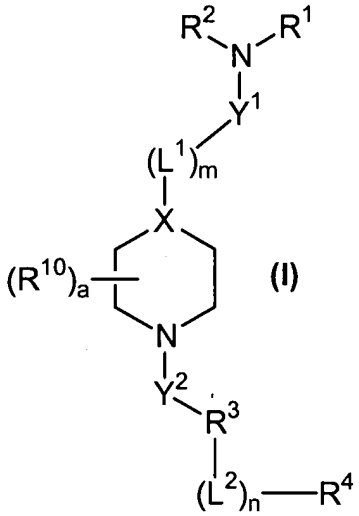


> Himmelsbach's compound has methyl whereas the instant *[sic invention]* has ethyl, propyl or benzyl on the amido nitrogen as R^1 and R^2. Himmelsbach, however, teaches that methyl, ethyl, propyl, isopropyl and benzyl are optional choices within a small genus of compounds (column 2, line 33; lines 50-53)."

and further that:

"... The compound of instant claims 2,3 has amino instead of Himmelsbach's cyano on the terminal phenyl. Himmelsbach, however, teaches that cyano and amino are optional choices (column 1, line 43). ... At the time of the invention, one of ordinary skill in the art would be motivated to replace Himmelsbach's cyano with the alternative amino to arrive at the instant invention with the reasonable expectation of obtaining an additional compound useful for inhibiting platelet aggregation since Himmelsbach had clearly taught that any species within the small disclosed genus would be effective as anti-aggregation agent."

Applicants respectfully traverse the rejection. Applicants submit that the instant application is directed to compounds of formula (I)



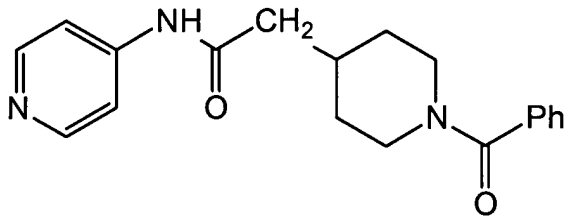
i.e. substituted piperidinyl derivatives wherein X is CH or $C(C_{1-6}alkyl)$, wherein the 4-position of the piperidinyl core is substituted with an aminocarbonyl- or aminocarbonyl-alkyl- group (or an aminothiocarbonyl or aminothiocarbonyl-alkyl- group) of the formula $-(L^1)_m-Y^1-N(R^1R^2)$, and wherein the 1-position of the piperidinyl core is substituted with a group of the formula $-Y^2-R^3-(L^2)_n-R^4$ wherein R^3 and R^4 are both required to be ring groups.

Himmelsbach discloses biphenyl derivatives, including more than 300 specific compounds. Of the more than 300 exemplified compounds, only 85 contain a substituted piperidinyl group, the majority of which are further substituted at the 4-position of the piperidine with an alkoxycarbonyl-alkyl- group. Only two of the more than 300 exemplified compounds are drawn to biphenyl derivatives containing a piperidinyl group, wherein the piperidinyl is substituted at the 4-position with an aminocarbonyl- or aminocarbonyl-alkyl- substituted piperidinyl (compound #82, column 27 and compound #6, column 34).

Additionally, Himmelsbach does not claim 1-biphenyl-carbonyl-, 4-aminocarbonyl- or 4-aminocarbonyl-alkyl- substituted piperidinyl compounds. Clearly, the teaching of Himmelsbach would not motivate one of ordinary skill in the art to make the aminocarbonyl- or aminocarbonyloalkyl-piperidine compounds claimed in the instant application. Thus, Applicants urge that the teaching of Himmelsbach does not render the present invention obvious and Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-4 and 10-12 under 35 U.S.C. §103(a).

The Examiner has rejected Claims 1-3 and 10-15 under 35 U.S.C. §103(a) as unpatentable over Sugimoto (USPN 4,895,841). More particularly, the Examiner states that:

> " Sugimoto generically discloses a acetylcholine-esterase inhibiting cyclic amine compound and the composition thereof (columns 2-3). Specific compounds are described on columns 55-56 (Table 4, compounds 48-50). Compound 49 has the following structure.



Sugimoto's example compound 49 does not have the instant $(L^2)_n$-R^4 substituent, such as phenylmethoxy, on the phenyl.
However, Sugimoto teaches that the presence or absence of substituents on the phenyl is an optional choice (column 8, line 39 to column 9, line 1) an example of phenylmethoxy-substituted phenyl is shown on columns 107-108, Example 237.

At the time of the invention, one of ordinary skill in the art would be motivated to replace Sugimoto's unsubstituted phenyl with the alternative, exemplified phenylmethoxy-phenyl to arrive at the instant invention with the reasonable expectation of obtaining an additional compound useful for inhibiting acetylcholinesterase ... and thereby useful for treating CNS disorder such as dementia."

Applicants respectfully traverse the rejection. As discussed in detail above, the instant invention is directed to substituted piperidinyl derivatives wherein the 4-position of the piperidinyl core is substituted with an aminocarbonyl- or aminocarbonyl-alkyl- group (or an aminothiocarbonyl or aminothiocarbonyl-alkyl- group) of the formula $-(L^1)_m$-Y^1-$N(R^1R^2)$, and wherein the 1-position of the piperidinyl core is substituted with a group of the formula $-Y^2$-R^3-$(L^2)_n$-R^4 wherein R^3 and R^4 are both required to be ring groups.

Applicants submit that Sugimoto discloses substituted piperidinyl compounds, including 249 specific examples. However, of the specific examples in Sugimoto, only four compounds (Examples 20, in column 43 and Examples 48, 49, 50 in column 55)

are substituted piperidinyl compounds wherein the 4-position is substituted with an aminocarbonyl-alkyl- substituent. These four compounds are substituted at the 1-position of the piperidinyl with a benzyl or phenyl-carbonyl substituent, rather than with a substituent containing two ring groups (*i.e.*, a group of the formula $-Y^2-R^3-(L^2)_n-R^4$) as required in the compounds of the instant invention. Further, more than half of the specific examples disclosed by Sugimoto (138 compounds) are compounds wherein the 4-position of the piperidine is substituted with an optionally cyclic, reverse amide, i.e. with a substituted carbonyl-amino-alkyl- group (*see, e.g.*, Example 5 & 6 in columns 34-35, Example 14 & 15 in column 40 and others).

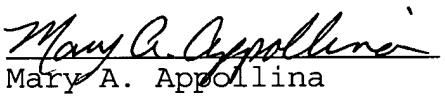
Additionally, of the specific examples in Sugimoto, only <u>one</u> compound of the 249 exemplified species (Example #237 in column 107-108) is a substituted piperidinyl compound wherein the substituent at the 1-position contains two ring groups. However, this compound does not have an aminocarbonyl- or aminocarbonyl-alkyl- substituent on the 4-position of the piperidine.

Applicants therefore maintain that the teaching of Sugimoto would not motivate one of ordinary skill in the art to make the compounds of the instant invention, i.e. substituted piperidinyl derivatives wherein the piperidinyl core is substituted at the 4-position with an aminocarbonyl or aminocarbonyl-alkyl group and wherein the 1-position is substituted with a substituent group of the formula $-Y^2-R^3-(L^2)_n-R^4$. Thus, Applicants submit that the teaching of Sugimoto does not render the present invention obvious and Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-3 and 10-15 under 35 U.S.C. §103(a).

The Examiner has objected to Claims 5, 7-9 and 16-18 as being dependent upon a rejected base claims. Applicants respectfully refer the Examiner to the above amendments and remarks and submit that the claims, as amended, are allowable and respectfully request that the objection be removed.

In view of the above remarks, Applicants maintain that the application is in condition for allowance and passage to issue is earnestly requested.

Respectfully submitted,



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